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VOL. 108 FEBRUARY, 1936 NO. 2

DEDICATION OF THE REMINGTON MEMORIAL LABORATORIES, THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

AT the Philadelphia College of Pharmacy and Science on January 31, as part of the annual conferences and exhibits in the sciences supporting the medical profession and the maintenance of health, the New Remington Memorial Laboratories were dedicated. The installation and equipment of these laboratories were made possible by the generosity of Mr. Josiah K. Lilly and Mr. Eli Lilly, of Eli Lilly & Company, Indianapolis pharmaceutical manufacturers, who are both graduates of the Philadelphia College.

At the evening program which followed the dedication, Dr. William Bosworth Castle, associate professor of medicine at Harvard

William Bosworth Castle, M. D.

University, received from the Philadelphia College the Procter Award in recognition of his notable contributions to the therapeutics and treatment of pernicious anemia. Dr. Castle addressed the meeting on recent developments in his field. He was presented for the award by Dean J. W. Sturmer, and the presentation was made by President Wilmer Krusen. Dr. George C. Yeager, president of the Philadelphia County Medical Society, presided at this meeting.

The significant features of the new Pharmacopœia were outlined by Dr. E. Fullerton Cook, chairman of the U. S. P. Committee of Revision, and those of the new National Formulary by Dr. Adley B. Nichols, secretary of the N. F. Committee of Revision. Dr. Horatio C. Wood, Jr., professor of pharmacology at the Philadelphia College, also spoke at this meeting on U. S. P. and N. F. medicines.

At the afternoon meeting, before the dedication of the new laboratories, the chemical fetaures, the biological features, the pharmacognosy and the pharmacy of the new U. S. P. were discussed by faculty members. Dr. Arthur Osol presented a paper on the U. S. P. chemicals, and Dr. Louis Gershenfeld on U. S. P. biological products and preparations for parenteral administration. Dr. Marin S. Dunn spoke on U. S. P. requirements for vegetable and animal drugs and Dr. Arno Viehoever on biological methods for standardizing cathartics. Dr. Viehoever also gave an illustrated lecture showing the action of various drugs on daphnia. The pharmacy of the new U. S. P. was discussed by Dr. Ivor Griffith and supported by a laboratory demonstration on the lecture platform.

In addition to the exhibition of the new laboratories in operation, there were exhibits at the College showing various types of U. S. P. and N. F. medicines and methods of preparing them. The uses of these preparations in dental practice and in hospital practice were also shown.

The model pharmacy which has been used a number of years at the Philadelphia College as a demonstration laboratory has been completely rearranged and was thrown open for the first time to visitors at this exhibit. The resulting rearrangement has created two model pharmacies. One illustrates the arrangement and equipment of a pharmacy devoted exclusively to the compounding of prescriptions and other professional services of pharmacy. In the other model pharmacy, the professional services of pharmacy are emphasized, but provision is made in the layout for the sale of other classes of merchandise which, though not strictly medicinal articles, are customarily

sold in many thousands of drug stores, and which are in harmony with the professional services which professional and lay patrons expect from a retail pharmacy.

Plans for the exhibit and the dedicatory ceremonies were under the direction of Dr. E. Fullerton Cook, who, in addition to being chairman of the U. S. P. Revision Committee, is also professor of operative pharmacy at the Philadelphia College and director of the pharmaceutical laboratories.

Therapeutic Action of Iron

A monograph in a recent issue of *The Lancet* (5862, 1), by L. J. Witts, deals with the factors affecting the requirement, absorption and utilization of iron. Recent work on the subject indicates that there is, for many patients, a minimal effective dose of iron. In addition to the physiological states which increase the requirement of iron, there are pathological conditions which impair its absorption and give rise to a "conditioned deficiency." The most important is acholor-hydria. The potentiating action of liver is highly complex, as liver is an acid food and a source of additional iron, copper, and pyrrol derivatives. Calcium is said to have an iron-sparing action, by which one must suppose promotion of absorption is meant, but the evidence is scanty. The author gives the following table showing average effective dose of common preparations of iron, and percentage of iron administered utilized for hæmoglobin formation:

Preparation	Daily dose in grams or cc.	Iron content in mgm.	Utilisation (per cent.)
Metallic—			
Ferrum redactum	1.5 to 6.0	1200 to 5000	0.5 to 2.0
Ferrous—			
Ferrous chloride	0.25 to 0.5	100 to 200	12.5 to 25
Ferrous sulphate exsic.	0.6	180	14
Ferrous lactate	1.5	300	8
Pil. ferri carb. (Blaud)	3.0 to 4.0	300 to 400	6 to 8
Ferric—			
Liq. ferri perchlor.	8.0	400	6
Ferric citrate	2.0	400	6
Idozan (ferric hydrox.)	30 to 45	1500 to 2250	1.1 to 1.7
Soluble ferric oxide	35	1000	2.5
Complex ferric—			
Ferri et ammon. cit.	4.0 to 8.0	800 to 1600	1.5 to 3.0
Injection—			
Inj. ferri B. P.	5.0 to 10.0	16 to 32	100

Only the non-hæmoglobin-like part of the iron of the food is available, and the hæmoglobin and similar compounds do not exert the therapeutic action of iron.

The therapeutic activity of preparations of iron by mouth is directly proportional to their solubility and to the ease with which they yield free ions of ferrous iron. Metallic iron, colloidal ferric preparations, and the scale preparations, in which the iron is in a complex form and not readily ionized, all require to be given in large doses to produce effects. The soluble ferrous salts are the most active. The average effective dose of ferric chloride has not yet been worked out with any degree of accuracy, but from some uncompleted experiments by N. S. Plummer and the author it must be higher than 400 mgm. of iron a day, equivalent to liq. ferri perchlor. 40 min. t. d. s. Incontrovertible evidence has been obtained that ferric chloride is less potent than ferrous chloride or ferrous sulphate. Solution of ferric chloride is intensely irritating, and the author found it quite impossible to use it in effective doses till he learnt the device of adding it to milk immediately before taking. The massive amounts of iron which must be ingested when reduced iron, colloidal ferric iron, or the scale preparations are used may cause indigestion, diarrhœa, cramps, and constipation, and even intestinal obstruction. There is also evidence that large amounts of unabsorbed iron in the intestine may interfere with the absorption of other minerals and vitamins. The ideal preparation of iron still awaits discovery.

(The use of the U. S. P. iron and ammonium citrates, orally or parenterally, has shown remarkable results in recent tests.)

Non-tarnishing Gilt

Gilt inks that will not tarnish may be obtained by the addition of barium and calcium bicarbonates, according to a recent report. It is stated that these salts have no adverse effect on normal paper size, and cause stabilizing conditions in the sheet so that none of the chemicals will exert a tarnishing influence on the inks when applied.

THE ANNUAL CONFERENCES AND EXHIBITS

ON THE SCIENCES SUPPORTING THE MEDICAL PROFESSION AND THE MAINTENANCE OF HEALTH

and

THE PRESENTATION OF THE PROCTER AWARD

in recognition of

Outstanding Achievements in These Sciences

at

The Philadelphia College of Pharmacy and Science

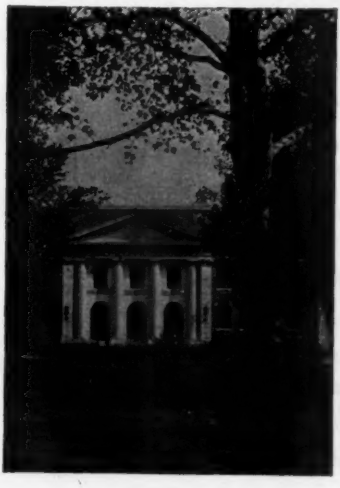
JANUARY 31, 1936

At 2:30 and 8:30 P. M.

ALSO

THE DEDICATION OF

THE REMINGTON MEMORIAL LABORATORIES



for

Undergraduate and Graduate Instruction

and for

Research in the Manufacture and Control

of

Pharmaceutical and Chemical Products

PROGRAM—2:30 P. M.

Dr. Wilmer Krusen—Presiding
President of the Philadelphia
College of Pharmacy and Science

The Newer Chemical Aspects of the Pharmacopœia
by Dr. Arthur Osol
Director of the Chemical Laboratories

Official Biological Products and the Official Preparations for Parenteral Administration
by Prof. Louis Gershenfeld
Professor of Bacteriology and Hygiene

Official Requirements for Vegetable and Animal Drugs
by Dr. Marin S. Dunn
Director of the Biological Laboratories

Biological Methods for Standardizing Cathartics
by Dr. Arno Viehoever
Research Professor in Biology

The Pharmacy of the U. S. P.
by Prof. Ivor Griffith
Associate Professor in Pharmacy

4:00 P. M.

DEDICATION OF
THE REMINGTON MEMORIAL LABORATORIES

Presented by
Mr. Josiah K. Lilly (P.C.P. 1882)
and
Mr. Eli Lilly (P.C.P. 1907)

Acceptance by
Prof. Charles H. LaWall
Dean of Pharmacy

Inspection of the Laboratories in Operation

In Lecture Room A

7:30 P. M.

Dr. Arno Viehoever will present Demonstrations of the Use of Daphnia as a Living Reagent; also moving pictures of the action of various drugs on Daphnia.

PROGRAM—8:30 P. M.

Dr. George C. Yeager—Presiding
President of the Philadelphia
County Medical Society

Presentation of THE PROCTER AWARD

to

William Bosworth Castle, M. D.
Associate Professor of Medicine
College of Medicine, Harvard University

In recognition of notable contributions to the Therapeutics and Treatment of Pernicious Anemia

Presented for the Award by Professor Julius W. Sturmer
Dean of Science

ADDRESSES

New Developments in the Products for the Treatment of Pernicious Anemia
by Dr. William Bosworth Castle

The Advantage of Official Medicines
by Dr. H. C. Wood, Jr.
Professor of Pharmacology

Significant Features of the New Pharmacopoeia
by Prof. E. Fullerton Cook
Chairman of the U. S. P. Committee
Revision, Director of the Pharmaceuti
Laboratories

The New National Formulary
by Prof. Adley B. Nichols
Secretary of the N. F. Committee of Revision, Ass't. Prof. of Operative Pharmacy

EXHIBITS IN THE FOYER

Booth 1—Official Medicines and Their Use in Extemporaneous Prescriptions
Booth 2—New Official Medicines, U.S.P. XI and N.F. VI
Booth 3—The Chemical Standardization of Official Medicines
Booth 4—The Biological Standardization of Official Medicines
Booth 5—Official Vehicles and their Use in Prescriptions
Booth 6—Official Medicines for Dental Use
Booth 7—Official Vegetable Drugs and Their Tests
Booth 8—Official Medicines in Hospital Practice and Other Useful Hospital Formulas

MODEL PHARMACIES

Second Floor, South Wing

2—A PHARMACY Equipped to Render Professional Service to the Community and to Physicians. (Using Finn-Iffland Fixtures and the latest Schwartz Prescription Department).

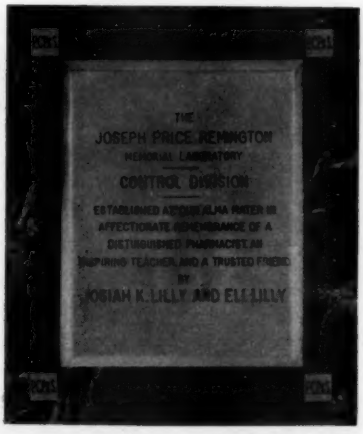
1—A PROFESSIONAL PHARMACY Demonstrating the Drugociu Prescription Department and associated scientific services such as Urine and Blood analysis, the preparation of Parenteral Solutions, Ophthalmic Preparations, Clinical Stains, etc.

Demonstrating the following departments:

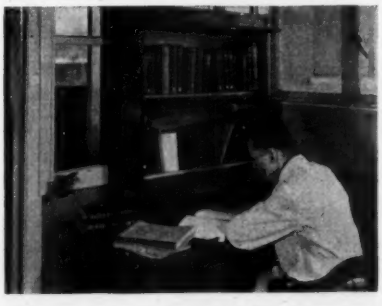
Prescriptions, Biologicals, Complete Insulin Service, Sickroom Supplies, Disinfectants and Antiseptics, Insecticides and Rodent Poisons, First-Aid Supplies, Simple Home Medicines, Surgical Supplies, Chemical Glassware and Reagents, Baby Needs, Soaps, Brushes, also other community services such as Perfumes and Cosmetics, Camera and Photographic Supplies, Stationery, Cigars and the Soda Fountain.

THE REMINGTON MEMORIAL LABORATORY

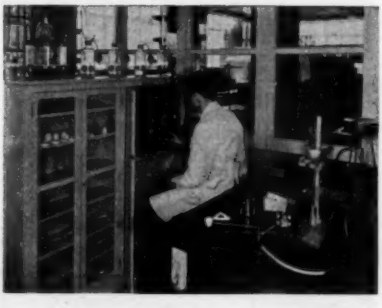
Second Floor—South Wing
Control Division



For the application of the official physical, chemical and botanical tests and assays used in the examination of ingredients and finished chemical and pharmaceutical products.



Office and Departmental Library



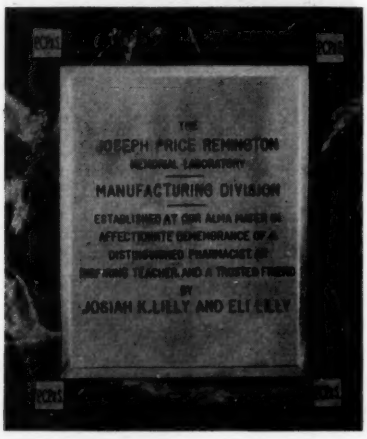
Facilities for Chemical Testing

Section for Physical and Botanical Testing

The Remington Memorial Laboratory (Continued)

Ground Floor—South Wing
Entrance on Woodland Avenue

Manufacturing Division



Experimental Extraction of Vegetable and Animal Drugs.

Standard Percolation.

Percolation with Vacuum and Pressure and Continuous Extraction.

Vacuum Dryer and Vacuum Still.

Vacuum and Lloyd Stills.

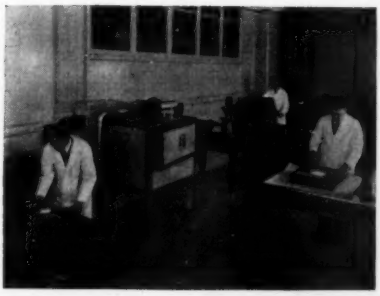
Open Evaporation.

Steam Boiler and Vacuum Pump.

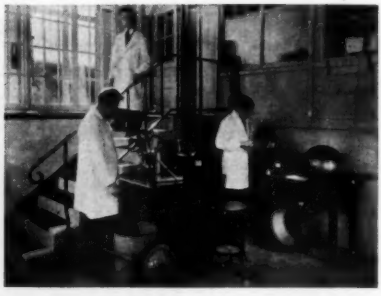
Weighing the Ingredients for a Formula

The Remington Memorial Laboratory (Continued)

Manufacturing Division



The Tablet Department



Tablet Coating and Filtration

Supply Department
Also Ointment Making and Tube Filling

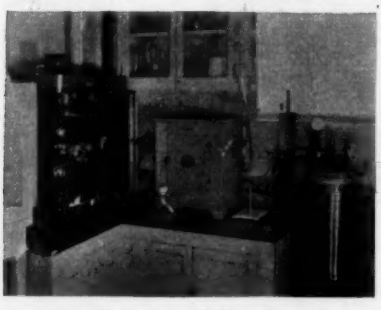
Emulsions by the Use of an Homogenizer
and the
Manufacturing Laboratory Office

A Laboratory for the Preparation of Solutions for Parenteral Administration and The Filling of Ampuls

(Presented by the Pharmacy Class of 1934)

Pyrex Glass Still Assembly for preparing "Ampul Water"

Preparing Solutions and Filling Ampuls



Sterilizers and Incubator

ORIGINAL ARTICLES

THE DEVELOPMENT OF REMEDIES FOR THE TREATMENT OF PERNICIOUS ANEMIA*

By W. B. Castle, M. D.†

PHILADELPHIA has long been recognized as the home of institutions of learning devoted to benevolent and practical purposes. The Philadelphia College of Pharmacy and Science illustrates well that aspect of the cultural spirit of the city to which I refer, for here the methods of science find expression in the study and standardization of remedies for the sick. As a physician, I can imagine no more useful advice in prescribing suitable and effective remedies than could be obtained by consulting a pharmacist of the type graduated by this institution. The addresses which we have heard and the demonstrations which we have seen today indicate the wide scope and the high ideals of this college. The dedication of the Remington Laboratories presented through the generosity of two graduates of this college, Mr. Josiah K. Lilly and Mr. Eli Lilly, is earnest of further progress in the controlled study and preparation of drugs. It is a privilege to be present on this distinguished occasion and a great pleasure to express my appreciation of the honor conferred on me by President Krusen and his associates in selecting me as a recipient of the Procter Award.

Medicine, which of all sciences is perhaps most concerned with results of immediate value to mankind, has certain objectives in common with pharmacy. The medical profession has reason to be grateful to the profession of pharmacy for the high and certified quality of drugs made available to the physician through the United States Pharmacopœia. Preparations of liver and stomach tissue for the treatment of pernicious anemia are for the first time described in the latest edition of the Pharmacopœia. The practical development of such preparations has benefited at many stages from the technical

*Address delivered at the Philadelphia College of Pharmacy and Science, January 31, 1936.

†From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) of the Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Mass.

co-operation of certain pharmaceutical manufacturing concerns. It may therefore possibly interest you to hear a brief account of the progress that has been made in the evolution of these remedies during the past decade.

Before 1926 pernicious anemia was almost invariably a fatal disease of only a few months' or a few years' duration. At that time Minot and Murphy (1) announced their famous discovery that the daily feeding of liver produced with regularity improvement in the blood and the clinical condition of patients suffering with pernicious anemia. Later it was shown that this improvement could be maintained so long as the patient continued to ingest 200 or more grams of liver daily. With a desire both to improve the convenience of the method and to determine the nature of the active constituent of liver, chemical fractionation was undertaken in collaboration with Dr. E. J. Cohn of the Harvard Medical School. The original procedures consisted in removing the proteins by heat and acidification, the further precipitation of proteins in alcohol of a strength of 70 per cent. by volume, and the production of a final precipitate in the alcohol filtrate by the addition of absolute alcohol in sufficient amounts to reach a concentration of 95 per cent. by volume. By 1927 this precipitate, known as "fraction G" and consisting of about 4.5 grams of a yellowish-brown powder derived from 100 grams of original liver, was shown to be therapeutically active (2). Further clinical observations showed that this material in amounts derived from 400 to 600 grams of liver, when given daily, was capable of producing maximal effects upon blood production and satisfactory clinical improvement (3). This was the first preparation of liver to become available to the medical profession. Subsequently Porter and his associates (4) developed an effective aqueous extract of liver by concentrating the filtrate resulting from the original precipitation of the liver proteins by heat. Connery (5) has successfully utilized fish livers in a similar process; and Davidson (6) has prepared effective fish liver extracts by a process similar to that used in the preparation of fraction G.

In further attempts at isolation of the active principle, Cohn, Minot and their associates (7) by 1929 had developed preparations sufficiently free of protein and of blood pressure-reducing substances to be given safely by intravenous injection. By 1930 a single injection of 0.48 gram of solids in solution consistently produced maximal effects upon blood production. In the same year West and Howe (8)

developed preparations which could be given intravenously with maximal effects in amounts of 0.3 gram of solids. These derivatives of fraction G were obtained from amounts of liver as large as 8000 to 25,000 grams.

In 1930 Gänsslen of Tübingen published apparently satisfactory results from the daily intramuscular injection of material derived from only 5 grams of liver. Since he did not describe the details of the method of preparation, confirmation of his work was rendered difficult. In 1931 Taylor, Strauss and I became interested in making comparisons of the effectiveness of a preparation which could be given either by oral or by parenteral administration. After numerous experiments upon animals which showed that the blood pressure-lowering principle present in fraction G had a persistence of action of only a few seconds, we came to the conclusion that a simple aqueous sterile solution of this material could be given safely to patients by slow intravenous infusion. Since relatively enormous doses of this material had been given to animals with no significant toxic effects, we cautiously administered to a suitable patient a neutral solution of 4.5 grams of fraction G derived from 100 grams of liver in 20 cc. of water. To our surprise a maximal effect on blood production resulted (10). Thereafter the work of Gänsslen was entirely confirmed with the demonstration that maximal effects upon blood production could be obtained from the daily intramuscular injection of the amount of fraction G derived from only 10 grams of liver (11). To produce similar effects upon oral administration, it is necessary to administer daily the same material derived from 400 to 600 grams of liver. Since then more concentrated preparations have been developed by Murphy and Clark (12). Recently Subbarrow, Jacobson and Fiske (13) have described a method which concentrates much of the activity of the original material by adsorbing on charcoal and subsequently eluting with alcohol. Strandell (14), working in Sweden, has reported the successful clinical use of extracts of liver prepared by Laland and Klem consisting of 0.001 gram of solid derived from 500 grams of liver. He states that a single injection of this material yields a striking effect upon blood production. Since the chemical methods have not yet been reported, it has not been possible to repeat his observations.

Active preparations of liver are soluble in water and in dilute alcohol. The activity is not destroyed by boiling in aqueous solution or by autoclaving for three hours at fifteen pounds' pressure. Hydrol-

ysis with dilute sulphuric acid renders the material inert. It readily passes through the Berkefeld filter or through collodion membranes. However, the nature of the active constituent is unknown. The results of the observations of Cohn, West and their respective associates indicate that it is probably a small nitrogenous base extremely low in alpha-amino nitrogen. Both Cohn and West have found that the activity is concentrated in a fraction precipitable by picric and flavianic acids.

It has long been known that the stomach in pernicious anemia is usually incapable of secreting hydrochloric acid or enzymes. Observations begun in 1928 by my associates and myself (15) have shown that in the normal human stomach a thermolabile substance (intrinsic factor) is secreted. This material reacts in the normal individual with a thermostable substance in the food (extrinsic factor). When suitable mixtures of the gastric and food factors are administered to patients with pernicious anemia, increased blood production, resembling that induced by liver or liver extracts, is produced. The absence of this reaction in the patient with pernicious anemia is considered to be the immediate cause of development of the disease.

In 1929 an important practical application of this work was made by Sturgis and Isaacs (16), who showed that the desiccated and defatted stomach tissue of the hog had therapeutic properties similar to those of liver. The activity of stomach tissue depends upon the presence of the two factors defined by our studies. The daily administration of 30 grams of desiccated stomach tissue derived from 265 grams of fresh stomach is capable of yielding maximal effects upon blood production. Wilkinson and his associates (17) have produced experimental fractions of hog stomach mucosa of such potency that similar effects upon blood production in pernicious anemia are produced by the daily administration of 5 grams of material. The available evidence suggests that the function of stomach preparations is to cause the formation within the body of the patient of substances similar to those contained in the liver, kidneys and other organs of normal animals and man. It is clear that the active principle or principles of stomach tissue are not identical with those of liver. For example, the activity of stomach preparations is destroyed by boiling for five minutes though such a procedure has no deleterious effect upon liver extracts (15).

An ingenious utilization of combinations of liver and stomach preparations has resulted from the work of Reimann (18) in Prague. He and his associates originally showed that the potency of fresh liver may be greatly enhanced by incubation with normal human gastric juice. As a result, Walden and Clowes (19) found that a mixture of animal gastric tissue with liver or with the liver fraction G resulted in an increase of potency greater than could be attributed to their combined activity. Reimann has shown that the daily administration of 4.5 grams of desiccated material derived from 10 grams of liver and 5 grams of gastric mucosa of the hog produces maximal effects upon blood production in pernicious anemia. In order to produce similar results, material derived from 265 grams of hog stomach or from probably more than 300 grams of liver would have to be administered daily. Autolysis of liver without the addition of gastric tissue does not result in an increase of potency as was at one time supposed. Although Gänsslen (20), Morris (21), Wilkinson (22), Conner (23) and others have reported stimulation of blood production by the parenteral injection of preparations of gastric juice or of gastric tissue, practical application of such products in the treatment of pernicious anemia has not been made. Indeed, it is not certain that the active principle of such preparations is specific for pernicious anemia since somewhat similar effects are obtainable by the oral administration of potassium arsenite (24) or the parenteral administration of materials containing protein or its derivatives (25).

Thus, in the ten years following the discovery of a means of treating pernicious anemia, efficient remedies both for oral and for parenteral use have been developed. For successful treatment it is therefore only necessary to administer enough of a given potent material at regular intervals. Within reason there is no danger from overdosage. Many patients remain in excellent condition when taking material by mouth. In others the necessary oral dosage may be so large that it is more convenient and less expensive to inject liver extract. The use of the parenteral route is especially indicated when complications such as arteriosclerosis, infections, or especially degenerative changes of the nervous system are present. Doubtless, more concentrated and hence more convenient preparations will be developed as time passes. Since it is possible that the substance responsible for relief of the anemia is not identical with that benefiting the nervous system, the possibility of an unsuspected loss of the latter with further purification must be kept in mind.

The present methods of treatment of pernicious anemia are reasonably convenient and entirely satisfactory provided effective preparations of the types described above are used. However, not all the products which the pharmacist may be urged to carry in his stock are equally effective. Preparations of weak or uncertain potency have already been made and sold by ignorant or unscrupulous manufacturers. This is a matter of serious consequence since lives may be lost or rendered a painful burden if the product prescribed for the treatment of pernicious anemia cannot be depended upon. The Council on Pharmacy and Chemistry of the American Medical Association has already taken steps to prevent such accidents by listing certain acceptable preparations. As mentioned above, the latest edition of the United States Pharmacopœia contains for the first time a description of preparations of liver and stomach tissues. Preparations of liver both for oral and for parenteral use in the treatment of pernicious anemia are described. Since different processes of manufacture retain different amounts of the original activity of the liver or of the stomach tissue in the final product, definition of the potency solely in terms of the amount of the original organ is obviously unsatisfactory. The potency of products meeting the standards of the United States Pharmacopœia will be defined in terms of the activity retained in the final product, irrespective of how much may have been lost in the process of manufacture. When the pharmacist supplies for the physician such a product both may have confidence in the effectiveness of that remedy and both should realize that the value of co-operation between their respective professions for the benefit of the sick has been further established.

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Sunburn Preventives

Certain quinine derivatives and glucosides of the aesculin type have long been used, though with indifferent results, in preventing sunburn. Latterly, benzyl salicylate in 25 per cent. concentration has had some vogue. Menthyl salicylate is said to be three times as effective, however. A 10 per cent. ointment of the latter is claimed to be exceedingly efficient. By the same token, salol (phenyl salicylate) should have some value in this direction.

Anti-oxidants

The impetus afforded to the study of oxidants, anti-oxidants and accelerators by the rubber industry in particular, has resulted in the application of such products elsewhere. In the preservation of animal fats such as lard (to retard rancidity) and cod liver oil (to retard vitamin destruction), in dyeing operations where prebleaching has affected the staple, and in many other directions the use of anti-oxidants is rapidly increasing.

A PHARMACOPŒIA FOR TODAY'S NEEDS*

By Professor E. Fullerton Cook
Chairman of the U. S. P. XI Committee of Revision

AN Efficient Medicine for Every Therapeutic Need. About a generation ago a new therapeutic era was ushered in under the stimulus of a group of earnest clinicians and pharmacologists who were greatly influenced by the relatively new evidences of drug action or inaction, through animal experimentation.

By some critics this group was termed "therapeutic nihilists," since they questioned the value of most drugs in the prevention or treatment of disease. One prominent clinician believed that only about a half dozen drugs were worthy of consideration since their physiologic activity could be demonstrated chemically or biologically.

Under the brilliant and able leadership of Dr. Osler the chairs of therapeutics were driven from most of the medical colleges and it has taken years to return to a reasonable and sound restoration of this important branch of medicine.

This process was revolutionary in nature and like all revolutions the proponents swung far to the left, questioning all traditions and empiricisms. Again history repeats itself and medicine is rediscovering the importance of "therapeutics" but basing this acceptance upon clinical evidence and scientific proof.

Tremendous advances have been made in the efficiency and specific character of many medicines during this period and the thousands of trained investigations in colleges and universities, in heavily endowed medical research institutions and in the research laboratories of a few of our pharmeceutical and chemical manufacturing firms, give much promise for the future.

During this revolutionary period the Pharmacopœia has kept pace with every development and the Eleventh Revision represents the clear-cut policy of its founder, Dr. Spalding, who, in 1820, stated that a Pharmacopœia to properly function must recognize the important medicines of its day. Unfortunately a few important medicines are excluded from the U. S. P. XI by the unwillingness of patentees to have their products included. Insulin and pentabarbital are in this group. It has been the policy of the present Committee of Revision to include a medicine for every therapeutic need when such is available.

*Read at the New York Branch of the American Pharmaceutical Association, January 13, 1936.

The New National Formulary contains preparations and standards for a number of these U. S. P. medicinal substances, especially as tablets or in parenteral solutions, or in nasal and throat preparations and elixirs.

The U. S. P. has taken the theoretical position that it should supply efficient therapeutic agents in such simple form that the physician could combine them in an original prescription to meet the needs of each patient.

In practice, however, the physician often finds it advantageous to use a form of combination prepared by skilled pharmacists, preparations having the correct proportion of medication and suitably flavored. For all such needs there should be an official preparation either in the U. S. P. or N. F. and the new revisions of both books are approaching this ideal.

Medicines of Superior and Uniform Quality and Potency. The letters "U. S. P." on a label should mean to physicians, pharmacists and the public a superior quality, adequate for every therapeutic need. An honest effort has been made to fix the standards of the Pharmacopœia so that a maximum of efficiency will always be obtained yet without the unnecessary cost due to the exclusion of the last traces of harmless foreign substances.

Furthermore a reasonable range must be permitted in U. S. P. standards to allow for the slight differences in analytical results obtained by even well-trained chemists and also because some deterioration is likely to occur even under the best storage conditions.

Scientifically Correct and Usable Titles. Some official titles have been criticized because of their cumbersome character and it must be admitted that it is difficult to learn and even to pronounce such titles as Erythrityl Tetranitrate but this is scientifically correct and had already been adopted by the British Pharmacopœia, and thus adds to the U. S. P. and B. P. uniformity. This has been a mutual policy for ten years.

In practice the Pharmacopœia has provided official abbreviations and often synonyms for use by physicians in prescribing, and there are advantages in the use of these which many physicians are recognizing. When titles are too short, euphonious and catchy, especially when they call for trade-marked and packaged medicines, the patient usually reads the prescription, buys it at a cut price store, and then,

if it has been efficient, recommends it to friends. This is not usually in the best interest of the health of the patients or the friends who thereafter are likely to dose themselves with that medicine indefinitely and unwisely. Physicians should learn and use official abbreviations when ordering medicines.

Efficient and Useful Vehicles. A wide variety of pleasantly flavored vehicles with different solvent properties are provided in the U. S. P. and N. F. Pharmacists should carry samples of these to physician friends and demonstrate their application. The various ointment vehicles and their specific uses should also be explained.

Research by Outstanding Scientists, both National and International. The independent and scientific position of the U. S. Pharmacopœia has always enabled it to command the cooperation of scientific workers throughout the country.

This feature has been greatly intensified during the past five years and the program now under way offers opportunities and insures results of far-reaching importance. Happily much of this is assuming international importance through the participation of the pharmacopœial commissions of other nations. Studies now under way deal with vitamins and anti-anemia products, these two being under the direction of special pharmacopœial advisory boards consisting of internationally known experts.

Another study deals with digitalis. This will be by clinicians and biological experts and will continue for several years. The help of the British Pharmacopœial Committee, the Swiss Pharmacopœial Commission and the Canadian experts is assured. Other studies dealing with pepsin standards and assay, aconite and ergot assays, soaps and antiseptic solutions, ointment vehicles, the extraction of drugs and the preservation of drugs and chemicals are among the researches under way.

Undelayed Revision of Standards by Interim Revision Whenever Necessitated by Scientific Advance. Although authorized by the Pharmacopœial conventions since 1900, the Committee of Revision rarely took advantage of the opportunity to revise the official standards between revisions. The wisdom and actual necessity for such revisions was faced by the committee several years ago and promptly accepted as an essential policy for a Pharmacopœia which was to meet the needs of today with its rapidly developing sciences. Four such "Interim Revisions" were released from 1933 to 1935, providing new standards

for Cod Liver Oil, Ergot, Lactoso, Oil of Lemon, Magnesia Magma, Bichloride Tablets and Non-destearinated Cod Liver Oil.

This policy has fully demonstrated its importance and with many new researches now actively in progress under Pharmacopœial supervision, with new facts being announced almost daily by the investigators in these related medical sciences, and with valuable new therapeutic agents being developed, the Pharmacopœia must of necessity adopt the plan of interim revision announcements. It is hoped that official announcements may be made from time to time as revisions or additions are decided by the committee, but that the printed text may take the form of an "Annual Supplement to the Pharmacopœia," appearing on January 1st of each year.

This plan would largely overcome the difficulty of securing publicity to changes, for the users of the Pharmacopœia would soon learn to expect a supplement yearly and would naturally consult the original Pharmacopœia and all of its supplements to determine the actual standards in force.

Prompt Recognition of New Medicinal Agents Whenever Their Merit Has Been Proven. The U. S. P. convention also authorizes the acceptance of additions to the Pharmacopœia whenever in the opinion of the committee the value of a new remedy justified such recognition.

It is not expected that this permission will be taken advantage of very frequently, for a medicinal product is not admitted to the Pharmacopœia until its importance has been widely recognized by the medical profession.

Products such as Insulin, unavailable until 1942 because of patent control, will undoubtedly be admitted as soon as the patent expires.

A serious problem for future Pharmacopœial committees will be the complications arising from the increasing tendency for universities and manufacturing firms to patent or trade-mark new medicinal products.

The policy followed by the committee up to this time has been the inclusion of meritorious new therapeutic agents of the patented or trade-marked class, only when the consent of the patentee or controlling factor had been obtained. When a product was controlled by and its distribution limited to one firm, even though consent to include in the U. S. P. had been granted, it was believed unwise to admit such substances.

This situation must be restudied and, if possible, some way devised whereby essential new medicines may receive Pharmacopœial recognition even though patented, otherwise the basic principle of the Pharmacopœia cannot be maintained namely that "it shall include the important therapeutic medicines of its day."

It was never intended that the inclusion of a product in the U. S. P. should in any way alter the legal rights granted an owner under patent or trade mark laws.

An Organized Program for Extending Reliable Information to the Medical Profession Concerning the Use of Official Medicines

(a) *Articles by Eminent Clinicians Suggesting Treatment for Specific Diseases.*

Through cooperation with the officials of the American Medical Association, one article of a series of twenty-four, will appear every two weeks for a year in the Journal of the A. M. A. These will deal with the use of official medicines in the treatment disease and will be written by leading medical men specially qualified for the presentation of each subject. The series will be subsequently published in one volume for the information of medical students, medical and surgical internes, and for physicians in practice.

Special articles will be presented on prescription writing and the use of official vehicles and typical prescriptions will be included.

(b) *Suggestions and Helps for Hospital Pharmacists and Pharmacists in General Practice in Extending Information to Physicians Concerning the Use of Official Medicines.*

A corresponding series of twenty-four articles will appear in pharmaceutical journals some weeks prior to the medical articles so that pharmacists and pharmaceutical manufacturers may emphasize to physicians the official products to be discussed and recommended in the forthcoming *A. M. A. Journal* articles. Pharmacists could even fill some of the typical prescriptions and show them to physician friends as an aid to them in prescription writing. This will be appreciated especially by some of the younger physicians who often lack confidence in the writing of prescriptions for official medicines where dosage, solubility, incompatibilities and vehicles are involved.

(c) *Exhibits for Medical Groups.*

It is also planned that an exhibit will be placed in the building of the Philadelphia County Medical Society presenting the preparations and prescriptions recommended in each of the *A. M. A. Journal* articles and these exhibits will be photographed and described for general publication and distribution to pharmacists and hospitals.

It is hoped that pharmacists in many localities will duplicate these exhibits before medical groups.

Pan-American Cooperation. It is gratifying to announce that the Pan-American Sanitary Bureau, through its director, Dr. Hugh S. Cumming, Surgeon General of the United States Public Health Service, and its assistant director, Dr. Boliver J. Lloyd, and their staff, have undertaken the translation of the U. S. P. XI into Spanish as an official activity of the Bureau. It is hoped that the Spanish edition will be available by April next when a large Pan-American Medical Congress will be held in this country.

It is also expected that the medical articles on the use of official medicines, appearing in the *A. M. A. Journal,* will be translated into Spanish and reprinted in the official bulletin of the bureau for circulation through the twenty-one republics affiliated in the Pan-American program.

It should be understood, however, that the policy of the U. S. P. Board of Trustees in translating the U. S. P. into Spanish now for four decades has been primarily that it might be available to pharmacists and physicians in Puerto Rico, the Philippines and in Cuba. In the latter republic the U. S. P. has been adopted as the official Pharmacopœia for more than thirty years and has been made possible through these years by the cooperation of the pharmacists of Cuba and the help of the scientific staff of the University of Havana and especially Dr. Jose Guillermo Diaz.

In the present revision, auxiliary commissions from Cuba, Puerto Rico and the Philippines have been participating in the revision (see the U. S. P. XI, page viii).

It is expected that each of the other republics affiliated with the Pan-American Union will eventually issue their own Pharmacopœia as is now done by Mexico, Brazil, the Argentine and others, but in offering the U. S. P. in Spanish it has been hoped that increased uniformity in nomenclature, tests and standards will be secured on this continent.

Thanks and Recognition for Those Who Have Made the U. S. P. Eleventh Revision

The U. S. P. Committee of Revision and Board of Trustees are deeply conscious and gratefully appreciative of the unprecedented loyalty, self-sacrificing labor and large financial help contributed by individuals and organizations during the revision of the Pharmacopœia.

This help has come not only from American physicians and pharmacists but from many in foreign countries. The close cooperation of the British Pharmacopœial Commission has been especially gratifying and points the way to far greater international participation in Pharmacopœial affairs. It is hoped that within the decade this may be realized by the establishment at Geneva, under the auspices of the Health Organization of the League of Nations, a secretaryship on Pharmacopœias. This is now under serious consideration.

A compilation is now being made of the contributions to the revision of the U. S. P. XI that suitable recognition may be given to those who have taken part in the program. It is only those who have demonstrated a willingness to contribute of their knowledge and time to the scientific or administrative work of the Pharmacopœia who have earned the right to actively participate in Pharmacopœial affairs; particularly must the Pharmacopœia be lifted from the level of politics.

THE NATIONAL FORMULARY VI

By Professor Adley B. Nichols

THE difference between the policies of the United States Pharmacopœia and the National Formulary is frequently misunderstood and should be clarified for the benefit of all. The U. S. P. is, and always has been, a national therapeutic guide, where one could rest assured that the accepted item was an efficacious product of proven value, regardless of how wide spread its use might or might not be. The N. F., on the other hand, makes no claims for therapeutic value, but bases its admissions upon the policy of general use. In both books, however, are found items known as pharmaceutical necessities, items possibly of no therapeutic value but required for the proper manufacture of some preparation. There should be no fear of rivalry between these two nationally accepted standards, for their policies are clean-cut and include the right of priority for the Pharmacopœia, should it desire to include an item previously recognized by or accepted for admission in the National Formulary.

Scope

The purpose and scope of the National Formulary is a question well worthy of first consideration, particularly in the case of the sixth edition which will become official June 1, 1936. The first three editions of the N. F. contained formulas for preparations only, the fourth edition, which appeared in 1916, being the first to provide standards for such simples as appeared in the formulas, but were not recognized in the U. S. P. Thus we find that the initial policy of providing monographs for preparations only was changed twenty years ago, and no one has questioned the wisdom of that step, for surely if uniformity of preparations was to be secured, uniformity in ingredients should first be provided.

After the appearance of the fifth edition of the N. F., one heard frequent comments to the effect that certain very popular simples were neither recognized in the U. S. P. nor in the N. F. If a preparation was recognized by the N. F. because of its general use, then why should not simples be recognized under similar conditions, particularly where they enjoyed even greater popularity by the medical profession than did some official preparations? Consequently the N. F.

VI revision committee gave consideration to the question of scope early in the course of revision, with the result that the new edition bears evidence of marked changes. The Committee made the slogan for admission to the N. F. VI "Use by the medical profession," and decided that simples should be included in the book if their use warranted such inclusion. The latter decision was looked upon with fear and skepticism by some who believed that it would mean a book double the size of the present volume. This fear was surely needless when we consider what actually happened. The policy of use governing admission, while an old policy, took on a new meaning however, for "use on hearsay" was not accepted but "use on fact" was required. These facts were obtained through several surveys, the largest one of which reviewed about 121,000 prescriptions collected from all parts of the country. In the face of such facts the committee was able to discard many "old timers," preparations which apparently had been allowed to remain for sentimental reasons only. The new N. F. contains 689 monographs, which is about 90 less than its predecessor. In all, 321 items of the N. F. V were not admitted to the N. F. VI, which is almost double the number deleted in the previous revision. A housecleaning such as this cannot help but bring the book into an up-to-date class. A total of 233 new items were admitted which is again a showing of marked improvement. Another forward step is the elimination of the old Part I, II and III arrangement, the new edition being patterned after the U. S. P. in that all monographs are arranged alphabetically, regardless of whether or not thy are for drugs, chemicals or preparations. Thus the book truly has been revised and should prove to be more useful and popular than ever before.

Vehicles

The vehicles of the N. F. have always been one of its outstanding features and the Sixth edition is resplendent with preparations which will aid the physician and dentist in making prescriptions more palatable. Most of you are probably familiar with the particular qualities of *Syrup of Cinnamon* in making the disagreeable taste of the salicylates and the fact also that its dark color tends to hide the too frequent darkening of a salicylate prescription. Pharmacists will also note with thanks the fact that the preparation is no longer made by the tedious process of percolation, but now is one of simple solution.

Syrup of Acacia is a new addition and is presented as a specific vehicle and not just as a suspending medium in the old sense of the term. Acacia represents a colloidal type of product in which disagreeable substances may be dispensed, the colloidal action of the acacia preventing, in a large measure, the contact of the medication with the taste buds. Its use with substances such as urea should receive special consideration. It is flavored with vanilla and preserved with sodium benzoate.

Syrup of Raspberry, which has received such splendid recognition for its masking qualities for the salty preparations such as the bromides, is again recognized. Fifteen grains of a bromide per teaspoonful makes one feel that a pinch of salt has been added to bring out the flavor of the syrup. In this connection it might be well to state that syrups in general serve as the best masks for salty items, rather than plain water or elixirs which in fact intensify the saltiness.

Syrup of Cherry is another new addition to the vehicle fold, and one which has received very wide acclaim where it has been available. Its specific value lies in its fruity tartness, which makes it a delightful mask for sour products such as the diluted acids, where the acid almost enhances the taste rather than destroy it. Unfortunately, the fact that the syrup is made from pure sour cherry juice and sugar will make it difficult at times to obtain the syrup in an off season. This difficulty should straighten itself out in time, as the pharmacist will be able to stock up during the period of plenty. This same situation holds true in the case of the raspberry syrup excepting that provision is made, with certain restrictions, for the use of a concentrate which is commercially available from some sources.

Aromatic Syrup of Eriodictyon is again recognized and particular attention is called to its value as a vehicle for bitter drugs such as quinine and strychnine. Eriodictyon has been used for years as a mask for similar items and Dr. Bernard Fantus (1) has shown how it forms an insoluble and therefore tasteless product which is later readily assimilated. Dr. Fantus has been responsible largely for a number of these new vehicles and reference to the literature on a number of these products (2) would be well worth while.

Other syrup vehicles worthy of mention are *Syrup of Prepared Cacao or "Chocolate Syrup,"* which has been definitely improved in flavor and texture. This offers a very heavy syrup for the suspension and subsequent masking of insoluble substances.

Syrup of Glycyrrhiza is now prepared from the fluid extract and highly recommended for salty preparations such as the bromides. The sweetness of the sugar itself is fortified by the sweetness of the glycyrrhizin.

Syrup of Thyme has a markedly "different" taste and is suitable for a change.

Many of the old vehicle elixirs, such as *Red aromatic elixir, Compound Elixir of Cardamon and Compound Elixir of Vanillin,* still remain available as general vehicles.

Iso-Alcoholic Elixir or *Iso-Elixir* however provides a new innovation. It consists of a high and low alcoholic elixir both resembling aromatic elixir in odor and taste, and offering unlimited possibilities in prescription work. If an aqueous type vehicle is desired, the low alcoholic elixir, which contains about 10 per cent. of alcohol, may be used, while the high alcoholic elixir with its alcoholic content of about 75 per cent. may be used for those substances which require a high percentage of alcohol for solution. The two elixirs are miscible and thus one may prepare a vehicle of any alcoholic strength between 10 and 75 per cent., dependent upon requirements. This feature has greater application than just to provide a solvent for a salt however. Everyone is familiar with the clouding produced when preparations like Tincture of Nux Vomica or Aromatic Spirit of Ammonia are prescribed with certain aqueous or even alcoholic vehicles.

With Iso-Elixir available, it is prescribed as the vehicle, and the pharmacist, in filling the prescription, adjusts the amounts of the low and the high elixir so as to produce a product of approximately the same alcoholic strength as the tincture of nux vomica for instance, thus preventing any clouding effect. This is a decidedly forward step in the attempt to produce more elegant prescriptions. For convenience in calculating, a table is given which will aid in determining the quantities of each elixir to use.

Ephedrine Preparations—Several preparations of ephedrine have been recognized in the N. F. VI, and these are simply called to your attention here as a matter for future reference as required. They are: *Jelly of Ephedrine Sulfate,* a 1 per cent. preparation in a tragacanth base; *Solution of Ephedrine Sulfate,* a 3 per cent. aqueous solution with chlorobutanol; *Ephedrine Spray* and *Compound Ephedrine Spray,* both 1 per cent. solutions in liquid petrolatum, the compound

solution also containing menthol, camphor and oil of thyme, while the plain contains a trace of methyl salicylate; finally a *Syrup of Ephedrine Sulfate* is also available. This contains 4 per cent. of the salt.

Dental Preparations

A very valuable group of preparations of the new N. F. is that dealing with dental products. An associate committee of the American Dental Association consisting of Drs. Blayney, Aiguier, Dailey, Freeman and Timmons were primarily instrumental in the selection of these products for inclusion in the book and from preliminary reports we already know that their selections are most valuable.

N. F. Dentifrice or N. F. Tooth Powder comes first in the dental group. This is a basic powder only, composed mostly of precipitated calcium carbonate with only a trace of soap (5 per cent.) and agreeably sweetened and flavored with a blend of soluble saccharin, oils of peppermint and cinnamon and methyl salicylate. This basic powder may readily be prescribed with sodium perborate or any desired medicament.

Glycerite of Iodine and Zinc Iodide, a modified or "Diluted Talbot's Solution" is next on the list. Every dentist is familiar with this popular preparation which has such marked antiseptic and astringent value in the treatment of pericementitis, gingivitis and lacerations.

Compound Dental Liniment of Aconite and Iodine is composed of 2 per cent. of iodine, 2½ per cent. of fluid extract of aconite and 3 per cent. of chloroform in a mixture of alcohol and water.

Odontalgicum is the official Latin title for what was previously a toothache wax but is now a liquid under the English title of *Toothache Drops.* It is a solution of chlorobutanol in oil of clove and is extremely efficacious, each of the ingredients having marked obtunding properties. It should prove of marked value as a first aid for toothache.

Compound Paste of Acetylsalicylic Acid, popularly called "Dental Anodyne Paste," is a splendid dental anodyne for tooth sockets. It contains eugenol, which has a definite obtunding effect, peruvian balsam, which is antiseptic and promotes granulation, and acetylsalicylic acid which acts as an anodyne. These are incorporated in a base of white wax and wool fat. The directions for manufacture must be

carefully observed lest the disagreeable separation of the balsam should occur, a problem which is familiar to most pharmacists and one which frequently causes difficulties.

Camphorated Phenol, composed of 30 per cent. of phenol and 60 per cent. of camphor in liquid petrolatum, is used as an antiseptic, devoid of topical irritation even to mucous membranes, in spite of its high phenolic content.

N. F. Aromatized Sodium Perborate is another one of the new dental items. It is agreeably flavored with oil of peppermint and soluble saccharin. Due to the large amount of this type of preparation being used by the layman without specific directions from a dentist or a physician, it might be well for the pharmacist to caution the customer about its promiscuous use when he sells the product. We realize how it has been the cause of severe mouth burns when used as a powder which lodges in cavities and eventually hydrolyzes to sodium hydroxide.

Solution of Procaine Hydrochloride, a sterile 2 per cent. solution of the salt in normal saline solution, is a popular dental anesthetic. Solution of epinephrine hydrochloride is usually added in small amounts just before use. The latter gives a bloodless working field and prolongs the action of the procaine.

One or two additional products are of particular interest to the dental profession. *Alkaline Aromatic Solution* is a standard mouth wash of an alkaline character. *N. F. Antiseptic Solution,* which as you note has a slightly changed title, has been fortified as far as its antiseptic properties are concerned by the addition of chlorthymol. A few minor changes have also been made in the formula.

Ampuls—Twenty-eight of the most popular ampuls are recognized in the new N. F. together with quite an elaborate general chapter, covering the question of the selection of glass for ampuls, the preparation of the solutions, the technic of filling, sterilizing and testing for sterility. The individual monographs do not contain specific formulas but contain tolerances, methods of sterilization and assay procedures. The tolerances are so worded that they apply to all sizes of ampuls. This section is a marked improvement for the book and places the manufacture of ampuls on the high plane where it rightfully belongs. Solutions for parenteral use should not be treated lightly,

for there is possibly no other form of medication so loaded with dynamite if it is not properly prepared.

A special monograph has been included on *Redistilled Water,* which is required for ampul solutions. It produces a water which is practically free from pyrogens, that protein substance which is the cause of so much fever, discomfort and anxiety when used parenterally.

Medicated Elixirs—In addition to the group of vehicle elixirs already mentioned, several new medicated elixirs have been placed in the N. F. VI.

Elixir of Aminopyrine contains about 2½ grains of aminopyrine to each teaspoonful. It is pleasantly flavored with orange and contains approximately 20 per cent. of alcohol. It has an attractive red color.

Elixir of Barbital, a dark brown elixir, flavored with the delightful compound spirit of vanillin, contains about 2 grains of barbital to each teaspoonful. The alcoholic content of the elixir is about 30 per cent.

Elixir of Phenobarbital is another of the new additions. It contains approximately ¼ grain of phenobarbital in each teaspoonful and is also red in color. Its alcoholic content is about 20 per cent. It too is flavored with orange.

Elixir of Sodium Thiocyanate, or, as it is frequently called, Elixir of Sodium Sulfocyanate or Sodium Rhodonate, has also been added to the medicated elixir group. It contains 2½ grains of the salt in each teaspoonful and is amber in color with a pleasant blended flavor.

Emulsions

Several cod liver oil emulsions have been continued, of which the one with egg offers the finest type of preparation. An additional popular emulsion has been added, namely, *Emulsion of Liquid Petrolatum with Phenolphthalein.* This is a 50 per cent. emulsion of heavy liquid petrolatum containing 1 grain of phenolphthalein to the average dose of a tablespoonful. It is emulsified with a combination of acacia and agar, so proportioned as to give a satisfactory product when prepared either by hand or by machine. The use of the hand homogenizer described is recent literature (3) produces an excellent product with

a minimum of effort and is a sure guarantee to the pharmacist against "broken" emulsions.

Glandular Products

Six glandular products have been recognized in the new N. F., namely *Corpus Luteum, Ovary, Ovarian Residue, Anterior Pituitary, Whole Pituitary* and *Suprarenal.* The newly developed histological characteristics of the glandular products, so well prepared by Dr. Heber Youngken of Boston, opens an entirely new field in this line of work.

Tablets

Another one of the outstanding new features of the N. F. VI is the section devoted to tablets in which 48 new monographs appear. As in the case of ampuls, the monographs are primarily prepared as a means of control for the enforcement authorities and to provide uniform standards for manufacturers. No specific formulas are given, but the individual monograph is devote to a tolerance statement worded so as to cover tablets of all sizes, tests for identity and purity, and a method of assay. For the most part, the tablets included are for simples only.

Miscellaneous

In addition to the many new items previously mentioned there are others of marked interest together with changes in old preparations, changes in titles and other general points of revision which can only be noted by a careful study of the book. Certain of the additional new monographs might be mentioned, however, and further details may be obtained later. Among these are *Solution of Boric Acid,* which is one of saturation; *Solution of Nux Vomica Alkaloids,* which is an aqueous solution prepared for veterinary use; *White Lotion,* which is the popular formula of the dermatologists and not the veterinary product as heretofore; *Syrup of Potassium Guaiacolsulfonate,* which contains about 5 grains of the salt per teaspoonful in aromatic syrup of eriodictyon; *Compound Ointment of Benzoic Acid,* or *Whitfield's Ointment,* which was greatly in need of uniform standardization; *Ointment of Coal Tar,* which contains 5 per cent. of coal tar in paste of zinc oxide; and finally *Ointment of Scarlet Red,* which contains 5 per cent. of scarlet red.

From the foregoing, it must be admitted that the new National Formulary has been markedly revised and has something of vital interest for every one concerned. The physician will find a solution to the ever-present question of how to improve the palatability of his prescription and he will also find many popular items made available with a standard, uniform formula, the same in Maine as in Southern California. The dentist will also take advantage of these same items and in addition, the numerous specialty preparations made available primarily for dental use. The pharmacist will be in a position to supply these items to the several professions and thereby help to further develop his own professional standing in his community.

REFERENCES

1. *J. A. Ph. A.*—April, 1933, p. 323.
2. *J. A. Ph. A.*—July, 1934, p. 698; *J. A. Ph. A.*—August, 1934, p. 812; *J. A. Ph. A.*—September, 1934, p. 915; *J. A. Ph. A.*—January, 1935, p. 46.
3. *A. J. P.*—April, 1935.

Schedule of Popular Science Lectures for 1936

Wednesday Evenings, 8.30 P. M.

February 19—*"Streamlines,"* George Rosengarten, Ph.D.

February 26—*"Out of Another Trash Can,"* Freeman P. Stroup, Ph.M.

March 4—*"Blood and the Criminal,"* Louis Gershenfeld, Ph.M.

March 11—*"The Trail of the Lonesome Pine,"* George Wesley Perkins, M.Sc.

March 18—*"The History and Romance of Digitalis,"* John E. Kramer, Ph.G.

March 25—*"Milestones in Chemistry,"* Arthur Osol, Ph.D.

April 1—*"Crystal Gazing,"* Ivor Griffith, D.Sc.

April 8—*"Elements of Flight,"* Charles Clifton Pines, B.Sc.

April 15—*"Lungs,"* Arno Viehofer, Ph.D.

April 22—*"Pulling the Trigger,"* William J. Stoneback, M.Sc.

April 29—*"National and International Standards for Medicine,"* E. Fullerton Cook, Ph.M.

May 6—*"Eggs—Scrambled and Unscrambled,"* Joseph W. E. Harrisson, Ph.M.

OFFICIAL REQUIREMENTS FOR VEGETABLE AND ANIMAL DRUGS OF THE U. S. P. XI AND N. F. VI

By Professor Marin S. Dunn

IT is impossible in the ten minutes allotted to me this afternoon to do more than touch upon some of the more striking changes apparent in the U. S. P. XI or N. F. VI and in a general way, by so doing, to indicate tendencies.

U. S. P. XI

I. Deletion of many crude drugs, about 28 in all, including Buchu, Calumba, Cimicifuga, Cubeba, Gambir, Hydrastis, Jalapa, Krameria, Quassia, Senega, Strophanthus and Uva Ursi.

II. Addition of Carbo Activatus (replacing Carbo Ligni), the residue from the destructive distillation of various organic materials treated to increase absorptive power; Digitalis Pulverata, an official powdered digitalis dried at a temperature not exceeding 60 degrees C. and reduced to a fine powder; and Stomachus, the dried and powdered defatted wall of the stomach of the hog, Sus scrofa var. domesticus Gray (Fam. Suidæ).

III. Changes designed for uniformity such as changing Belladonnæ Folia to the singular number.

IV. Changes in certain definitions. Some of these changes are corrections of botanical origins and author citations. Others deal with the admission of synthetic camphor, dropping of Cape Aloes, recognition of Jamaica Ginger only. Stem and root barks both specified in Red and Yellow Cinchona, etc.

V. Changes in, or specification of, moisture content limits—Agar (16 per cent. now 18 per cent.); Digitalis, Ergot (8 per cent. limit, introduced); Gentiana, 10 per cent. (introduced).

VI. Changes in per cent. extractive requirements—Kino, Ipecacuanha, Zingiber. Kino yields not less than 60 per cent. of alcoholic-soluble extractive and not less than 75 per cent. water-soluble extractive (from 45 per cent. and 80 per cent.).

VII. Changes in allowable ash—Acacia, Lycopodium, Myrrha. Acacia 0.5 per cent. acid-insoluble ash; Lycopodium 0.75 per cent acid-insoluble ash; Myrrha 5 per cent. acid-insoluble ash from 4 per cent.).

VIII. Changes in other purity requirements: Aspidium, not less than 1.5 per cent. crude filicin; Podophyllum, not less than 4 per cent. of resin of podophyllum; Nux Vomica yields not less than 1.15 per cent. of strychnine (from 2.5 per cent.).

IX. Improved Potency Definitions, Digitalis and Ergot.

Digitalis: The potency of Digitalis shall be such that 0.1 gm. of it, when assayed as directed, shall possess an activity equivalent to not less than 1 U. S. P. digitalis unit.

Ergota: Ergot, when assayed by the method herein directed, possesses a potency, per gram, equivalent to not less than 0.5 milligram of ergotoxine ethanesulfonate.

X. Changes in percentage of allowable foreign organic matter in cases of certain drugs: Althæa, Cascara Sagrada, etc. Althæa not more than 1 per cent. (new). Cascara Sagrada not more than 4 per cent. (new).

XI. Correction, clarification and amplification of descriptions both macro and microscopic of a large number of articles. The histological characters of thyroid are given.

XII. Addition of new identity tests—Acacia (polarization), Myrrha HNO_3, Br_2 vapor).

XIII. Addition of new purity tests—Acacia, water-insoluble residue. Zingiber (test given under Assay U. S. P. X).

XIV. Directions for storage are given in a number of cases: Camphora, Ergota, Prunus Virginiana, etc., and the animal drugs, Cantharis, Posterior Pituitary, Thyroid and Stomachus.

Other changes such as Official Latin Titles (Tolu = Balsamum Tolutanum), Official English Titles (Balsam of Peru = Peruvian Balsam) and synonyms (Carum = Caraway Fruit) have not been mentioned.

N. F. VI

I. Inclusion of a chapter on General Notices.

II. Information is easier to find because of improved format.

III. Deletion of a large number of crude drugs (fifty-seven in all), including Asclepias, Cypripedium, Hæmatoxylon, Myrica, Pimenta, Quercus, Solanum, Thuja and Zedoaria.

IV. Addition of twenty-six new articles dealing with crude vegetable drugs (many of which come from U. S. P. X; Buchu, Calumba, Cimicifuga, Gambir, Hydrastis, Jalapa, Krameria, Quassia, Strophanthus, Uva Ursi, etc.). In addition, the following animal drugs become official: Corpus Luteum, Ovarium, Pituitarium Anterior, P. Totum, Residuum Ovarii and Suprarenalum.

V. A number of changes (six) in Latin Titles: Euphorbia changed to E. Pilulifera; Gossypii Cortex—Gossypii Radicis Cortex, etc.

VI. A number of changes (twelve) in English titles: Juniper Berry changed to Juniper; Saffron to Crocus; White Pine Bark to White Pine, etc.

VII. Changed definitions (a) changes from plural to singular: Calendula, Castanea, etc.; (b) Sanguinaria (roots omitted in definition), Trillium (roots added to definition), etc.

VIII. Changes in per cent. extractive requirements: Cacao Præparatum (not more than 22 per cent. non-volatile ether-soluble extractive), Populi Gemma (not less than 40 per cent. anhydrous alcohol-soluble extractive).

IX. Limits of permitted acid-insoluble ash given for each drug usually not more than 2 per cent, but exceptions in the cases of Crocus 1 per cent., Foeniculum 1.5 per cent., Guarana .5 per cent, Iris 1 per cent., Kola .5 per cent., Mastiche .25 per cent., Matricaria 4 per cent.

X. Improved Potency Standard:

Convallariæ Radix, when tested by the prescribed method, possesses a potency such that 0.1 gm. of it is equivalent to 3 U. S. P. digitalis units, U. S. Pharmacopœia XI, page 136.

Strophanthus, when assayed by the prescribed method, possesses a potency, per gram, equivalent to not less than 55.0 mg. of standard ouabain, U. S. Pharmacopœia XI, page 486.

XI. A number of changes in permissible foreign organic matter—particularly the specification of limits of other foreign organic

matter than the extraneous parts of the article in question. For example:

Apocynum—limit of 2 per cent. on other foreign organic matter beside the stem bases of Apocynum (5 per cent.).

Eupatorium—not more than 10 per cent. of the stems of the plant and not more than 2 per cent. of other foreign organic matter, etc.

XII. Changed Descriptions:

(a) Many changes tend toward conciseness, accuracy and clarity.

(b) In certain cases, paragraphs have been rewritten or new paragraphs added, depending upon the individual need for treatment. For example:

Cacao Præparatum—Description rewritten.

Populi Gemmæ, Sumbul—Added paragraphs on Structure, etc.

XIII. Added purity and identity tests. For example:

Chondrus—tests for sulphites; Crocus—compositæ florets test, etc.

XIV. Assays included in articles for Chionanthus, Colchici Cormus, Coriandrum, vanilla, etc. Crocus and Persio have color assays.

XV. Storage and Preservation.

Directions given for Cacao Præparatum, Cactus, Grandiflorus (using alcohol), Vanilla. Directions omitted for Cataria and Taraxacum.

XVI. Cautions for Apocynum and Euonymus reworded and in italics.

XVII. Under the new animal articles, besides definitions, standards for purity, directions for storage, descriptions of the histological elements are added (making it necessary for the Pharmacognocist to become familiar with animal histology.

Conclusion

Great attention has been given to the production of two modern, scientific reference works, which are clearly written, accurate, comprehensive, and at the same time concise as possible.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Linwood F. Tice, M. Sc.

A Source of Loss of Ammonia in Kjeldahl Distillations. H. S. Miller, *J. Ind. Eng. Chem. Anal. Ed. 8,* 50 (1936). In the Kjeldahl distillation process the first portions of ammonia liberated are so diluted with air as to escape complete absorption in the standard acid. This loss is quite appreciable as shown by a series of experiments in which 25 cc. portions of ammonium chloride solution, containing in each 25 cc. 35 mg. N, were subjected to the ordinary technic of Kjeldahl distillation. An average loss of 1.26 per cent. was experienced. The loss was clearly due to entrainment of ammonia by air inasmuch as ammonium chloride solutions boiled to exclude air before the addition of the alkali gave results which were only negligibly different from the theoretical.

The nature of the ordinary Kjeldahl distillation as applied to sulfuric acid solutions makes such technic impractical and consequently the tube through which the ammonia is delivered into standard acid was so constructed as to break up the air bubbles in order that they might allow the more complete absorption of the ammonia. The delivery end of the tube was closed and flattened and ten holes each 0.08 mm. in diameter were made in the bottom of the tube.

Using this type of delivery tube, results were obtained which were removed from the theoretical by only 0.03 per cent. Under conditions comparable to a regular Kjeldahl distillation an average deviation of only 0.06 per cent. lower than the theoretical was found.

Alkali Therapy of Hypersecretion and Hyperacidity. K. P. Becker, *Deut. Arch. klin Med. 177,* 115 (1935) through *C. A. 29,* 5518 (1935). Neutralon (a sodium aluminum silicate) was found to decrease both the volume (by about 25 per cent.) and the acidity (about 21 per cent.) of the gastric secretion. In hyperacidic subjects the effect persists for about twenty-four hours and it is not merely a neutralization but more far-reaching.

Sodium bicarbonate and magnesium peroxide did not reduce the acidity of the gastric secretion and actually, in some cases, both the volume and the acidity were increased as much as 50 and 55 per cent. respectively.

The Water Capacity of Ointment Bases. Pharm. Acta Helv. 10, 163 (1935). A knowledge of the water absorption capacities of various ointment bases is of obvious importance.

The experimental procedure used in this study was the incorporation of the maximum amount of water possible in a melted base followed by cooling and removal of the excess water. The amount of water held by the base was then determined by a tetrachlorethane distillation procedure and the separated water measured.

The "water number" of the various ointment bases was then calculated in the following manner:

$$\begin{aligned} &\text{Weighed amount of saturated base} = A \\ &\text{Water content} = B \\ &\text{Weight of base alone} = A - B \\ &\text{Water number} = \frac{100\ B}{(A - B)} \end{aligned}$$

Various samples of vaseline gave water numbers from 9.3 to 15.6. The addition of from 5-40 per cent. of spermaceti increased somewhat the values with the optimum concentration arising at 5 per cent.

Cetyl alcohol increased the water number of vaseline considerably, the optimum amount being approximately 4 per cent. which gave a water number of from 38.88 to 51.51 depending upon the variety of the cetyl alcohol employed.

With wool fat an unusual result was obtained in that the water numbers of mixtures of vaseline and wool fat containing 5, 10, and 15 per cent. of the latter all were identical, namely, 78.57. The incorporation of more than 5 per cent. of wool fat with vaseline in order to increase its capacity for water absorption is hereby proven useless. Wool fat itself gave a water number of 475 but on aging in a refrigerator the product separated water and finally a value of only 185.7 was indicated.

The P. H. V Unguentum cetylicum, a combination of 4 p. cetyl alcohol, 10 p. wool fat, and 86 p. white petrolatum, showed a water absorption capacity ranging from 81.81-108.3 with various samples of white petrolatum.

Hydrogenated arachis oil gave a water number of 75.43 which was increased to 170.3 by the addition of 1 per cent. of cetyl alcohol. With 3 per cent. of cetyl alcohol a maximum value of 185.71 was otbained. With large amounts of water these combinations were quite

hard in consistence. Wool fat increased the water number of hydrogenated arachis oil only slightly.

The efficiency of cetyl alcohol was further illustrated with lard whose water number was increased from 7.52 to 244.89 by the addition of only 3 per cent. Wool fat in a ratio of 1-5 increased the water number to 112.76.

White wax in an optimum concentration of 10 per cent. increased the value of a sample of lard from 9.28 to 26.58. Increasing the amount of wax lowered quite considerably the water number.

Several additional observations were made by the authors concerning which reference should be made to the original article.

The Production of Tablets and Their Significance as Pharmaceutical Preparations. P. Kämpf, *Pharm. Acta Helv. 10,* 195 (1935). This article treats in a general way of the production of tablets and the important qualities which they should possess. Attention is drawn to it specifically because of its excellent collection of references on tablets, chronologically arranged from 1762 to 1935. Approximately five hundred references are cited from a wide variety of American and foreign journals. One who is interested in the literature on tablets will find this tabulation of great value.

The Preparation and Preservation of Morphine Injections. H. Davis, *Quart. J. Pharm. Pharmacol. 8,* 683 (1935). This investigation was conducted in behalf of the British Pharmacopœia Commission to develop a formula for an injection of morphine capable of resisting contamination when exposed to the varying conditions of army use.

Morphine tartrate was found to be no more susceptible to the development of mold growth than the hydrochloride, but the latter was considered the more desirable because it can be sterilized in an autoclave.

Inasmuch as the solution was to be available in containers from which successive doses could be withdrawn, a preservative was essential. Parachlormetacresol was found to provide a satisfactory pre-

servative action in a concentration of 0.1 per cent. which was sufficient to render the injection solution sterile without the necessity of an additional heat treatment. Solutions made with parachlormetacresol may be autoclaved with some slight loss in the efficiency of the preservative.

Tests for freedom from abnormal toxicity as prescribed by the Therapeutic Substances Regulations, 1931, were made with 0.2 per cent. w/v solution of parachlormetacresol and no serious symptoms were produced.

A Modification of the Benedict's Qualitative Test. J. Fine, *Brit. Med. J. 1,* 1169 (1935) through *Quart. J. Pharm. Pharmacol. 8,* 722 (1935). Five cc. portions of Benedict's Qualitative solutions are placed in each of two test tubes. To one of these is added 0.5 and to the other 0.1 cc. of the urine under examination. Both tubes are then placed in a boiling water-bath for exactly five minutes. The contents of each tube are then filtered and examined for the presence of blue color due to unreduced copper. If the original urine contained less than 2 per cent. glucose, a blue color should be seen in both filtrates; if it contained more than 2 per cent. of glucose the blue color should be seen only in the second filtrate. The actual percentage can be roughly estimated by comparison with standards prepared from glucose solutions in water, of known strength, which have been prepared in exactly the same manner, and then sealed. Such standards appear to keep for several months. A modified Benedict's solution containing 1.61 per cent. of $CuSO_4.5H_2O$, 16.1 per cent. of sodium citrate and 9.3 per cent. of anhydrous sodium carbonate is recommended.

The Therapeutic Use of Helium in Asthma. C. K. Maytum, L. E. Prickman and W. M. Boothby, *Proc. Staff Meetings Mayo Clinic 10,* 788 (1935) through *Squibb Abstr. 9,* 110 (1936). Mixtures of helium and oxygen in the approximate ratio of 1:2 are claimed to be of considerable value in the treatment of asthmatic attacks which cannot be controlled by the usual measures and also certain others in which cyanosis is not relieved by a 4:1 oxygen nitro-

gen mixture. In severe asthma the commonly employed drugs such as epinephrine and morphine are practically useless. Results with the helium-oxygen mixture were quite successful, cyanosis disappearing rapidly with a relaxation on the part of the patient. No marked ill effects have been observed although slight reactions may occur such as headache, dryness in the upper air passages or a metallic taste in the mouth. The beneficial effect is attributed to the ready diffusibility of the mixture.

Percolation of Cinchona and Belladonna Root. A. W. Bull, *Quart. J. Pharm. Pharmacol. 8,* 378 (1935). The percolation of cinchona in a moderately fine powder was found to give better extraction of both alkaloids and total extractive than was obtained with either a fine powder or a moderately coarse indicating that an optimum degree of comminution exists for percolation of this drug. The ratio of alkaloids to other solids increased in successive fractions of percolate. It was also shown that grading the comminuted drug into various sized powders and packing the percolator so that the finer particles were on top gave the most satisfactory extraction results. Such a procedure exposes the finest powder which is the most difficult to extract to fresh menstruum.

With belladonna root an analogous result was obtained as to optimum particle size but successive portions of the percolate gave a decreasing ratio of alkaloid to other extractive showing that in this drug the alkaloids are more easily extracted than other components.